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(54) A Medicated Wipe

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(54) Title: A MEDICATED WIPE

(57) Abstract

A wipe, comprising an absorbent woven or non-woven fabric, cloth or tissue substrate, impregnated with a pharmaceutically active agent, wherein the agent is a substance effective in stimulating melanocytes to produce melanin and/or is effective in a topical treatment of a skin condition in combination with electromagnetic radiation falling in the range of 220-700nm.

A MEDICATED WIPE

DESCRIPTION

This invention relates to an absorbent wipe or swab, impregnated with a pharmaceutically active agent, or other material, for use in applying, by wiping, the agent or other material to the skin.

Medical or cleansing wipes, each comprising an absorbent woven or non-woven fabric or cloth, a woven or non-woven cellulosic tissue or web, or the like, impregnated with an aqueous or alcoholic solution of a detergent, perfume, antiseptic, a locally active anaesthetic, an antihistamine, a rubefacient, or a carboxylic acid (as a virucide), are known and disclosed in at least British Patent Nos. 1565775; 2103089 and; 2190289. Such wipes are normally supplied individually wrapped in sealed sachets or pockets which, for example, can be formed by sandwiching an impregnated and folded wipe between two larger sheets of an aluminium foil/polyethylene film laminate and heat welding the sheets of laminate together, around the periphery of the folded wipe.

Medicated and non-medicated emollient compositions, for use in treating dermatological disorders in which the abnormal skin is exposed to ultraviolet light (UV), preferably to UVA, are disclosed in International Patent Application No. PCT/GB92/00556. Such compositions can include, as active agents, substances effective in stimulating melanocytes to produce melanin, such as a psoralen or urocanic acid, the preferred psoralens being 8-methoxypsoralen and trimethylpsoralen. The described emollient compositions are lipophilic non-viscous liquids which, on application to skin or a like surface, spread to provide a substantially uniform coating of lipophilic emollient, which is sufficiently non-volatile to persist, once spread, for a significant period of time. The compositions can comprise a lipophilic emollient in admixture with a polar solvent and a surfactant.

When used, medicated emollients of the aforementioned type are generally spread over an extensive area of the body and it has been proposed, therefore, to apply the same using spray applicators (see the aforementioned International Patent Application). However, if the emollient composition includes an active agent, such as 8-methoxypsoralen, which has the potential for being systemically toxic, it has now been found that this method of application can be significantly disadvantaged. For example, precautions must

be taken to prevent the aerosol, produced by the applicator, from entering the eyes and other body orifices of patients and healthcare workers exposed thereto. Also, in order to prevent prolonged and uncontrollably repeated exposure to psoralens, which can lead to the absorption of harmful quantities of such an agent, healthcare workers who regularly treat patients with compositions including psoralens, using spray applicators, must wear cumbersome protective clothing. The risks, in fact, are of sufficient significance to make it unsafe for patients to use spray applicators for self-applying such medicated compositions.

The present invention is intended to offer a solution to at least some of these problems.

According to the present invention there is provided a wipe, comprising an absorbent woven or non-woven fabric, cloth or tissue substrate, impregnated with a pharmaceutically active agent, wherein the agent is a substance effective in stimulating melanocytes to produce melanin and/or is effective in a topical treatment of a skin condition in combination with electromagnetic radiation falling in the range of 220-700nm, which, preferably, is UV (285-400nm) and more preferably is UVA (320-400nm).

In a second aspect, the invention provides a wipe comprising

an absorbent woven or non-woven fabric, cloth or tissue substrate, impregnated with an emollient composition comprising a lipophilic emollient, wherein the composition is a non-viscous liquid which, on application to the skin or a like surface, spreads to provide a substantially uniform coating of the lipophilic emollient, which coating does not absorb a significant amount of incident therapeutic radiation within a predetermined band width and is sufficiently non-volatile to persist for a period of sufficient length, for a therapeutically effective dose of said therapeutic radiation to be administered. Preferably, the therapeutic radiation is UV (285-400nm) and, more preferably UVA (320-400nm).

Wipes in accordance with either aspect of the invention can be employed to apply the pharmaceutically active agent, or emollient composition, to the skin, with minimal risk of the applied material accidentally entering the eyes or other body orifices of either patients or healthcare workers. Thus, even when an active agent having the potential to be systemically toxic is so applied, the need for protective clothing is minimised; the maximum protection required to use a wipe in accordance with the invention can be as little as a surgical or like glove, worn on the hand in which the wipe is held.

In an embodiment of the first aspect of the invention, the pharmaceutically active agent is selected from 8-methoxypsoralen, trimethylpsoralen, 6-methoxypsoralen, 3-carbethoxypsoralen, cis-urocanic acid, trans-urocanic acid, mixtures of cis- and trans-urocanic acids, and amino oxoaliphatic carboxylic acids wherein the aliphatic skeleton has 4-1[illegible] carbon atoms (including the carboxy carbon), the amino group is primary, or is a secondary or a tertiary alkyl amino group, and is γ, or preferably δ, or further from the carboxy carbon and the oxo group is β, or preferably γ, or further from the carboxy carbon. The preferred δ-amino oxoaliphatic acid is δ-aminolevulinic acid (5-amino, 4-oxopentanoic acid). The active agent, preferably, is dissolved in a suitable carrier or solvent. Preferably, the aliphatic skeleton has 5-10 carbon atoms, more preferably 5-8 carbon atoms and most preferably 5 or 6 carbon atoms.

Preferably, wipes in accordance with the invention are suitable for use in the topical treatment of psoriasis, or other skin disorders in which the stratum corneum becomes flaky or scaly, including mycoses fungicides, and acne vulgaris, alopeica areata, dermatitis herpetiformis, eosinophilic pustular folliculitis, erythrokeratoderma (symmetrical and progressive), chronic lichenoid GVH disease, granuloma annulare, histiocytosis X, ichthyosis

linearis circumflexa, lichen planus, pityriasis lichenoides, pityriasis rosea, pityriasis rubra pilaris, pressure sores, pruritis (primary and secondary), seleromyxoedema, subcorneal pustular dermatoses, transient acantholytic dermatoses, and atopic eczema.

The method of treatment employed can be as described in International Patent Application No. GB92/00556.

Where the active agent is a δ-amino oxoaliphatic carboxylic acid, such as δ-aminolevulinic acid, the electromagnetic radiation used, preferably, is in the visible spectrum, more preferably excludes any UV radiation and, most preferably, is largely in the range of 600-700nm. Such active agents can be employed in emollient compositions which absorb significant amounts of UV radiation.

In a preferred embodiment of the first aspect of the invention, the pharmaceutically active agent is dispersed or dissolved or dispersed in an emollient composition of the type employed in the second aspect of the invention. Preferably, the emollient composition is of a type disclosed in International Application No. PCT/GB92/00556.

Thus, the emollient composition, used in either aspect of the invention, can comprise a non-volatile and relatively

thick lipophilic emollient dissolved in a carrier. The lipophilic emollient, preferably, should not absorb a significant amount of instant therapeutic radiation and, preferably, after application to healthy normal skin, the emollient transmits through to the skin 90% or more and, more preferably, 95% or more incident UVA, UVB or broad band UV.

Preferably, the lipophilic emollient is chosen so that a 5μm layer thereof absorbs 20% or less and, preferably, 10% or less of the incident therapeutic radiation. Preferably, a 5μm layer of the lipophilic emollient absorbs 20% or less and, more preferably, 10% or less incident radiation at any wavelength within the broad band UV, UVA or UVB regions of the electromagnetic spectrum.

In this specification broad ban UV is defined as radiation of a wavelength between 285 and 400 nm, UVA has a wavelength of 320-400 nm and UVB a wavelength of 285-320 nm.

In a preferred embodiment the composition has a viscosity of between 5 and 20,000 centipoise and, preferably, a viscosity of between 5 and 2,500 centipoise. Preferably, the lipophilic emollient has a partial vapour pressure of 17.5mmHg, or less, and preferably, 10mmHg, or less, at 20°C. Also, it is preferred that the partial vapour pressure of a

coating formed by the composition on skin or a like surface, should be 17.5mmHg, or less, and preferably, 10mmHg, or less, at 20°C, for a period of sufficient length for a therapeutically effective dose of incident radiation to be administered.

The lipophilic emollient is, preferably, in admixture with a carrier having the property of enhancing the spreadability of the emollient composition, to assist in the formation of an even and unbroken coating of the lipophilic emollient. The preferred carriers are non-polar solvents, including volatile silicone oils, such as cyclomethicone, octamethylcyclotetrasiloxane (ABIL K4, available from Goldschmidt GmbH of Essen, Germany), decamethylcyclopentasiloxane (ABIL B8839, available from Goldschmidt GmbH of Essen, Germany), a dimethicone, or a mixture of any of these. The carrier can comprise a surfactant, which can be isopropylisostearate, pentaerythratol tetraisostearate, promyristyl propionate, myristyl lactate, oleyl erucate, isorpropyl myristate, isocetyl stearate, isopropyl isostearate, other aliphatic esters of fatty acids or a mixture of any of these.

The lipophilic emollient, preferably, is coconut oil, sesame oil, sunflower oil, corn oil, a mineral oil, such as liquid paraffin or a fraction thereof, or any other like saturated

oil or a mixture of any of these, and, more preferably, is coconut oil.

Most preferably, the pharmaceutically active agent is carried in a vehicle which includes singly or a mixture of:-

(i) a vegetable oil or oils, such as coconut arachis or palm kernel;

(ii) a mineral oil or oils;

(iii) a volatile silicone oil or oils, such as octamethylcyclotetrasiloxane or decamethylcyclopentasiloxane; and

(iv) an aliphatic ester of a fatty acid, such as isopropyl myristate or isopropyl isostearate.

In further embodiments, a coloured or UV disclosing dye is included with the pharmaceutically active agent, to act as a marker, showing where the latter has been applied.

The preferred material for forming the wipe substrate is cotton lint and the impregnated wipe is, preferably, sealed into an enveloping sachet or pocket. Preferably, the sachet or pocket is formed by sealingly sandwiching a folded and impregnated wipe between two sheets of an aluminium foil/polyethylene film laminate. The sheets of laminate may comprise folded over portions of a single sheet of such material.

The preferred psoralen is 8-methoxypsoralen or trimethylpsoralen and is included in a concentration of between 0.0125% and 10% and, preferably, 0.0125% and 0.1% by weight. The other listed active agents can be used in similar amounts, although the δ-amino oxoaliphatic carboxylic acids can be used in concentrations of up to 15% by weight.

Specific embodiments of the present invention will now be described, by way of illustration only.

Example 1

100gms of natural coconut oil is blended with 100gms of isopropyl isostearate and 100gms of cyclomethicone, to provide a non-viscous liquid composition. The composition is divided into four equal parts and 8-methoxypsoralen was added to these in the following amounts:-

(a) 0.0125% by weight;

(b) 0.025% by weight;

(c) 0.05% by weight and;

(d) 0.1% by weight.

4ml aliquots of each of the resulting solutions (a)-(d) are deposited onto 10cm x 10cm cotton lint sheets and each sheet is then sealed into a pouch, formed from a laminate of aluminium foil and polyethylene film.

Example 2

A non-viscous liquid composition, prepared in the manner described in Example 1, is divided into four equal parts and δ-aminolevulinic acid was added to these in the following amounts:

(a) 0.05% by weight
(b) 1% by weight
(c) 5% by weight
(d) 10% by weight.

4ml aliquots of each of the resulting solutions (a)-(d) are deposited onto 10cm x 10cm cotton lint sheets and each sheet is sealed into a pouch, formed from a laminate of aluminium foil and polyethylene film.

Example 3

To use a wipe, prepared in the manner described in Example 1 or 2, it should be removed from its pouch or sachet and wiped over the area to be treated with incident electromagnetic radiation, in order to apply a thin and uniform coating of the coconut oil and 8-methoxypsoralen, or δ-aminolevulinic acid.

Once coated in a composition, prepared in accordance with the instructions set out in Example 1, a patient, suffering

from psoriasis, is subjected to UVA treatment of between 2 and 5 minutes in a conventional UVA light cabinet, after which the composition may be washed off. Treatment normally involves 2-3 such exposures for 4-8 weeks, until the diseased areas have reverted substantially back to normal. Thereafter, the disease may be held in check by a maintenance regime of 1 PUVA treatment per week over an indefinite period.

Whole body light cabinets which are suitable for use in the manner set out are listed in P.J. Mounford, "Phototherapy and PhotoChemotherapy Ultraviolet Irradiation Equipment", Photodermatology 1986:3:83/91. The exact exposure times for each particular light cabinet should be determined by a responsible clinician in the normal manner.

Psoriasis patients can be treated in a similar manner with compositions prepared in accordance with the instructions set out in Example 2, excepting that the radiation employed is in the visible spectral region and can be applied at a dose of between 10 and 50 J/m^2 at a power density of about $70mW/cm^2$.

CLAIMS

1. A wipe comprising an absorbant woven or non-woven fabric, cloth or tissue substrate, impregnated with an emollient composition comprising a lipophilic emollient and a pharmaceutically active agent, wherein the active agent is a substance effective in stimulating melanocytes to produce melanin and/or is effective in a topical treatment of a skin condition in combination with therapeutic eletromagnetic radiation falling in the range of 220-700nm, and is selected from 8-methoxypsoralen, trimethylpsoralen, 6-methoxypsoralen, 3-carbethoxypsoralen, cis-urocanic acid, trans-urocanic acid, mixtures of cis- and trans-urocanic acids and amino oxoaliphatic carboxylic acids in which the aliphatic skeleton has 4-10 carbon atoms, the amino group is primary, or is a secondary or tertiary alkyl amino group, and is γ, or preferably δ, or further from the carboxy carbon and the oxo group is β, or preferably γ, or further from the carboxy carbon, the composition is a non-viscous liquid which, on application to skin, spreads to provide a substantially uniform coating of the lipophilic emollient and active agent, and the coating does not absorb a significant amount of incident therapeutic eletromagnetic radiation within the range of 220-700nm and is sufficiently non-volatile to persist for

a period of sufficient length, for a therapeutically effective dose of said electromagnetic radiation to be administered.

2. A wipe as claimed in claim 1, wherein the amino oxoaliphatic acid is a δ-amino oxoaliphatic acid and, preferably, is δ-aminolevulinic acid.

3. A wipe as claimed in claim 2, wherein the therapeutic electromagnetic radiation is in the visible spectrum and, preferably, is in the range of 600-700mn.

4. A wipe as claimed in claim 1, wherein the pharmaceutically active agent is 8-methoxypsoralen.

5. A wipe as claimed in claim 4, wherein the therapeutic electromagnetic radiation is UV, in the range 285-400nm, or preferably UVA, in the range 320-400nm.

6. A wipe as claimed in claim 1, wherein the therapeutic eletromagnetic radiation is broad band UV, UVA or UVB radiation, the emollient composition is anhydrous and has a viscosity of between 5 and 2500 centipoise, and the lipophilic emollient, when spread in a 5μm layer, absorbs 10% or less of the incident therapeutic eletromagnetic radiation and has a partial vapour pressure of 10mmHg or less, at 20°C.

7. A wipe as claimed in any of claims 1-5, wherein a 5μm layer of the lipophilic emollient absorbs 20% or less incident therapeutic eletromagnetic radiation.

8. A wipe as claimed in claim 7, wherein a 5μm layer of the lipophilic emollient absorbs 10% or less incident therapeutic eletromagnetic radiation.

9. A wipe as claimed in any of claims 1-5, 7 and 8, wherein the emollient composition has a viscosity of between 5 and 20,000 centipoise and, preferably, between 5 and 2500 centipoise.

10. A wipe as claimed in any of claims 1-5 and 7-9, wherein the lipophilic emollient has a partial vapour pressure of 17.5mmHg or less, preferably 10mmHg or less, at 20°C.

11. A wipe as claimed in any of claims 1-5 and 7-10, wherein the partial vapour pressure of a coating, formed by the emollient composition on skin, is 17.5mmHg or less, preferably 10mmHg or less, at 20°C.

12. A wipe as claimed in any of claims 1-11, wherein the emollient composition further comprises a carrier for the lipophilic emollient.

13. A wipe as claimed in claim 12, wherein the carrier

comprises a substantially non-polar solvent.

14. A wipe as claimed in claim 13, wherein the carrier is a volatile silicone oil, preferably selected from cyclomethicone, octamethylcyclotetrasiloxane, decamethylcyclopentasiloxane, a dimethicone, and mixtures of any of these, or is cyclomethicone.

15. A wipe as claimed in claim 13 or 14, wherein the carrier comprises a surfactant.

16. A wipe as claimed in claim 15, wherein the surfactant is selected from isopropylisostearate, pentaerythratol tetraisostearate, promyristyl propionate, myristyl lactate, oleyl erucate, isopropyl myristate, isocetyl stearate, isopropyl isostearate, mixtures of any of these and other aliphatic esters of fatty acids.

17. A wipe as claimed in any of claims 1-16, wherein the lipophilic emollient is selected from coconut oil, sesame oil, sunflower oil, corn oil, a mineral oil, such as liquid paraffin or a fraction thereof, mixtures of any of these, or preferably is coconut oil.

18. A wipe as claimed in any of the preceding claims, impregnated with a pharmaceutically active agent carried in a vehicle which comprises, singularly or in admixture:-

(i) at least one vegetable oil;

(ii) at least one mineral oil;

(iii) at least one volatile silicone oil;

and

(iv) at least one aliphatic ester of a fatty acid.

19. A wipe as claimed in claim 18, wherein the vegetable oil is coconut erachis and/or palm kernal oil, the volatile silicone oil is octamethylcyclotetrasiloxane and/or decamethylcylopentasiloxane and the aliphatic ester of a fatty acid is isopropyl myristate and/or isopropylisostearate.

20. A wipe as claimed in claim 1, wherein the pharmaceutically active agent is 8-methoxypsoralen or trimethoxypsoralen and is included in a concentration of between 0.1 to 5% and 10%, or preferably betweem 0.0125% and 0.1% by weight.

21. A wipe as claimed in claim 1, wherein the pharmaceutically active agent is δ-aminolevulinic acid and is included in a concentration of up to 15%, or preferably up to 10% by weight.

22. A wipe as claimed in any of the preceding claims for use in a topical treatment of a skin condition in combination with electromagnetic radiation, wherein the skin condition is psoriasis, acne vulgaris, alopecia

areata, dermatitis herpetiformis, eosinophilic pustular folliculitis, erythrokeratoderma (symmetrical and progressive), chronic lichenoid GVH disease, granuloma annulare, histiocytosis X, ichthyosis linearis circumflexa, lichen planus, pityriasis lichenoides, pityriasis rosea, pityriasis rubra pilaris, pressure sores, pruritis (primary and secondary), seleromyxoedema, subcorneal pustular dermatoses, transient acantholytic dermatoses, or atopic eczema.

23. A wipe as claimed in any of the preceding claims, sealed into an enveloping sachet or pocket.

24. A wipe as claimed in claim 23, wherein the sachet or pocket is formed by sealingly sandwiching a folded and impregnated wipe between two sheets of an aluminium foil/polymer film laminate.

25. A wipe as claimed in claims 1 and 9, for application to the skin of a subject for treating a dermatological disorder, capable of forming a uniform layer of the lipophilic emollient and active agent on the skin of said subject with a thickness of approximately 5μm, said layer being transparent to 80% of a wavelength of therapeutic radiation selected from broad band UV, UVA and UVB, at said thickness, and having a partial pressure less than or equal to 17.5mm Hg at 20°C, said composition being for application prior to said subject receiving a

therapeutically effective dose of incident radiation and said layer remaining on said skin, during the administration of the therapeutically effective dose of incident radiation, to direct radiation to the epidermis.

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